APPENDIX A

UNITED STATES COURT OF APPEALS
FEDERAL CIRCUIT

Nos. 03-1193, -1210

HOUSEY PHARMACEUTICALS, INC.,
Plaintiff-Appellant,
v.

ASTRAZENECA UK LTD., ASTRAZENECA LP, ASTRAZENECA PHARMACEUTICALS LP, AND AVENTIS PHARMACEUTICALS, INC.,
Defendants-Cross Appellants,

and

BRISTOL-MYERS SQUIBB COMPANY,
Defendant-Cross Appellant,

and

MERCK & CO., INC.,
Defendant-Cross Appellant,

and

ROCHE HOLDINGS, INC., HOFFMANN-LA ROCHE INC., ROCHE LABORATORIES, INC., AND SYNTEX (U.S.A.) INC.,
Defendants,
and WYETH AND WYETH PHARMACEUTICALS, INC.,
Defendants-Cross Appellants.

[May 7, 2004]

Before MAYER, *Chief Judge*, NEWMAN and CLEVENGER, *Circuit Judges*. Opinion for the court filed by Circuit Judge CLEVENGER. Dissenting opinion filed by Circuit Judge PAULINE NEWMAN.

CLEVENGER, *Circuit Judge.*

Housey Pharmaceuticals, Inc. ("Housey") sued Astrazeneca UK Ltd., Astrazeneca LP, Astrazeneca Pharmaceuticals LP, Aventis Pharmaceuticals, Inc., Bristol-Meyers Squibb Co., Merck & Co., Inc., Roche Holdings, Inc., Hoffmann-La Roche Inc., Roche Laboratories, Inc., Syntex (U.S.A.) Inc., Wyeth, and Wyeth Pharmaceuticals, Inc. (collectively "defendants") in the United States District Court for the District of Delaware, alleging infringement of four patents addressing methods of screening for protein inhibitors and activators. The district court construed several of the limitations of the patent claims, including "inhibitor or activator of a protein." *Bayer Ag v. Housey Pharm., Inc.,* No. 01-148-SLR, 2002 WL 31833205 (D.Del. Nov. 12, 2002).[1] Housey subsequently stipulated that, if this construction were not reversed or modified on appeal, its patents would be invalid and not infringed. *Housey Pharm., Inc. v. Abbott Pharm., Inc.,* No. 01-401-SLR (D.Del. Nov. 26, 2002). The district court ordered a final judgment of invalidity and noninfringement. *Housey Pharm., Inc. v. Abbott Pharm., Inc.,* No. 01-401 SLR (D.Del. Nov. 27, 2002). We conclude that the district court's construction of "inhibitor or activator of a protein" was not erroneous, and we therefore affirm the judgment.

I

Housey is the owner by assignment of U.S. Patents No. 4,980,281, No. 5,266,464, No. 5,688,655, and No. 5,877,007, all of which are titled "Method of Screening for Protein Inhibitors or Activators." Concerning the limitation "inhibitor or activator of a protein," the parties treat the use of the

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[1] The order containing the district court's constructions of the disputed limitations carries a different caption because the court consolidated oral argument on claim construction in the instant case with a co-pending matter involving the same patents.

limitation in claim 1 of the '281 patent as representative, and we do likewise:

> 1. A method of determining whether a substance is *an inhibitor or activator of a protein* whose production by a cell evokes a responsive change in a phenotypic characteristic other than the level of said protein in said cell per se, which comprises:
>
> (a) providing a first cell line which produces said protein and exhibits said phenotypic response to the protein;
>
> (b) providing a second cell line which produces the protein at a lower level than the first cell line, or does not produce[] the protein at all, and which exhibits said phenotypic response to the protein to a lesser degree or not at all;
>
> (c) incubating the substance with the first and second cell lines; and
>
> (d) comparing the phenotypic response of the first cell line to the substance with the phenotypic response of the second cell line to the substance.

'281 patent, col. 24, ll. 46-63 (emphasis added).

The patented method is an assay, or test, to determine whether a substance, often a candidate for a pharmaceutical product or drug, is an "inhibitor or activator" of a particular protein (the "protein of interest" or "POI") in a cell. Steps (a) and (b) of the method require the existence of two different cell lines. One cell line produces more of the POI, and the other produces less, or none, of the POI. (The cell line producing more of the POI is sometimes referred to as the "test" cell line, and the cell line producing less or none of the POI is sometimes referred to as the "control" cell line.) Additionally, the two cell lines are differentiated by the fact that the increase in the amount of the POI in one of the cell

lines modifies some characteristic in that cell line. In the language of claim 1 of the '281 patent, the relevant characteristic of each of the cell lines is labeled a "phenotypic response" to a different concentration of the POI, and the difference between the relevant characteristic in the two cell lines (presumably caused by the increase in the POI) is a "responsive change in a phenotypic characteristic." In step (c) of the method, the substance being screened is added to each of the cell lines. Step (d) requires comparing the effect that the substance has on the phenotypic response to the POI in each cell line.

In Housey's words, the method requires treating the two cells "with a test substance to determine whether that substance inhibits the cellular functioning of the POI . . . as measured by modulations of the responsive change in the phenotypic characteristic of [one] cell, compared with the modulations of the same responsive phenotypic characteristic, if any, in the [other] cell." The method is allegedly valuable because if the substance being screened impacts the phenotypic response of the cell with an increased concentration of the POI and does not affect the cell containing less or none of the POI in the same way, a logical guess is that the substance has this differential impact because the substance has an effect on the POI. This knowledge is valuable: If a POI is believed to be implicated in a certain disease, and a substance is known to affect that POI, then the substance is more likely to have some value in treating the disease than another substance which does not affect the biological activity of the POI.

II

The district court conducted a *Markman* hearing and construed five claim terms disputed by the parties, including

"inhibitor or activator of a protein,"[2] which was held to mean "a substance that has a greater effect on the phenotype of cells that express the protein of interest at a higher level than on the phenotype of cells that express the protein of interest at a lower level or not at all."

The district court considered and expressly rejected Housey's argument that an "activator or inhibitor of a protein" was limited to substances that "directly interact [with], *i.e.*, bind to, the target protein." The interpretation adopted by the district court includes within an "inhibitor or activator of a protein" substances that affect the test cell's "responsive change in a phenotypic characteristic" through the direct-binding concept to which Housey argues the term is absolutely limited. In addition, however, it is broader: it includes substances that operate through other indirect concepts of molecular interaction. For example, under the district court's interpretation, a substance being screened may still be an "inhibitor or activator of a protein" if it binds to and alters the metabolic functioning of a molecule other than the POI that is essential to either a biochemical pathway required to produce the POI in the first place or a biochemical pathway in which the fully formed POI participates in the cell in order to trigger the "phenotypic response." In other words, the district court's definition includes within the scope of an "inhibitor or activator of a protein" substances that inhibit or activate the biological activity of the POI in the cell without binding to the POI itself.

Housey stipulated that, "based upon the Court's construction of the claim limitation 'inhibitor or activator of a protein,' . . . [and] subject to its right to appeal the Court's

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[2] The district court's constructions of the other four disputed claim terms are contested either by Housey in its appeal, or by the defendants in a conditional cross-appeal. Because our holding on the construction of "inhibitor or activator of a protein" is dispositive by virtue of Housey's stipulation, we do not address these other terms.

claim construction and any final judgment based thereon, that the Court may enter an order stating that the patents in suit are invalid and not infringed." Housey and the defendants, however, "reserve[d] all of their claims, counterclaims, arguments and defenses" if "the Court's determinations on . . . issues of claim construction [related to 'inhibitor or activator of a protein'] are reversed or modified on appeal such that the matter is remanded for further consideration." Based on the stipulation, the district court entered final judgment in favor of the defendants.

Housey appealed to us, and we have jurisdiction to hear the appeal pursuant to 28 U.S.C. § 1295(a)(1).

III

We review the district court's claim construction de novo. *Cybor Corp. v. FAS Techs., Inc.,* 138 F.3d 1448, 1456 (Fed. Cir.1998) (en banc). Claim construction begins with the language of the claims. *Johnson Worldwide Assocs., Inc. v. Zebco Corp.,* 175 F.3d 985, 989 (Fed. Cir.1999). When construing patent claims, there is a "heavy presumption" that the language in the claim "carries its ordinary and customary meaning," *CCS Fitness, Inc. v. Brunswick Corp.,* 288 F.3d 1359, 1366 (Fed. Cir.2002), "amongst artisans of ordinary skill in the relevant art at the time of the invention," *ResQNet.com, Inc. v. Lansa, Inc.,* 346 F.3d 1374, 1378 (Fed. Cir.2003). Dictionaries and treatises may provide insight into a term's ordinary meaning thus defined. *Tex. Digital Sys., Inc. v. Telegenix, Inc.,* 308 F.3d 1193, 1202-03 (Fed. Cir.2002). However, a claim must also be considered in the context of the intrinsic evidence, namely the claims, the specification, and the prosecution history. *Rexnord Corp. v. Laitram Corp.,* 274 F.3d 1336, 1342-43 (Fed. Cir.2001). If there is a discernable plain and ordinary meaning of the claim language, then this meaning usually defines the scope of the claims unless the patentee has explicitly disclaimed or clearly disavowed this meaning in the specification or prosecution

history. *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir.2004) (requiring "words or expressions of manifest exclusion or restriction" before broad terms in a claim will be read narrowly in light of a narrow specification (quoting *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1327 (Fed. Cir.2002)); *Middleton, Inc. v. Minn. Mining Mfg. Co.*, 311 F.3d 1384, 1388 (Fed. Cir.2002) ("This court also considers the prosecution history . . . to determine whether the applicant clearly and unambiguously 'disclaimed or disavowed [any interpretation] during prosecution in order to obtain claim allowance.'") (quoting *Standard Oil Co. v. Am. Cyanamid Co.*, 774 F.2d 448, 452 (Fed. Cir.1985) (alteration in original)). For example, the patentee may act as his own lexicographer and expressly define the term in the specification. *See Tex. Digital Sys.*, 308 F.3d at 1204; *Rexnord*, 274 F.3d at 1342.

A

The language of claim 1 of the '281 patent clearly supports the district court's construction and is inimical to any narrower construction. The claim recites "[a] method of determining whether a substance is an inhibitor or activator of a protein." '281 patent, col. 24, ll. 46-47. The steps of the method in turn permit a determination of whether substances affect phenotypic response to the POI in the test and control cells differently. Thus, if "a substance . . . has a greater effect on the phenotype of cells that express the protein of interest at a higher level than on the phenotype of cells that express the protein of interest at a lower level or not at all," the substance is, as defined by the claimed method itself, an inhibitor or activator of the protein of interest.

Furthermore, the specification expressly defines an "inhibitor or activator of a protein" as a substance that yields a positive response to the claimed method, just as the district court did. *See id.* at col. 3, ll. 5-10 ("Substances which specifically inhibit or inactivate [sic] the POI may be dis-

tinguished from substances which affect cell morphology or growth by other mechanisms in that they will have a greater effect on the test lines than on the control line."); *id.* at col. 4, ll. 48-50 ("Inhibitors or activators are identified by their greater effect on the phenotype of the higher producing cell line.").

Housey argues that the district court's construction "confuses the method of distinguishing activators or inhibitors with the definition of activators or inhibitors." We disagree. The claim addresses a method of determining whether a compound is an inhibitor or activator that is conducted by observing whether a particular event occurs when the method is performed. It is therefore logical to construe an "inhibitor or activator of a protein" as a substance that precipitates that event, especially given that the specification, too, defines an inhibitor or activator in the same way.

B

Housey's principal argument on appeal with respect to the construction of "inhibitor or activator of a protein" is the same one that was rejected by the district court: Housey argues that this limitation is "properly construed to mean substances that interact with, *i.e.,* bind to, the POI in order to exert their inhibiting or activating effect on the cellular functioning of the POI." We do not agree that, as used in the '281 patent, an "inhibitor or activator of a protein" is limited to substances that achieve their effect on the biological activity of the POI through a particular reaction mechanism, namely binding to the POI. A substance need only have "a greater effect on the phenotype of cells that express the protein of interest at a higher level than on the phenotype of cells that express the protein of interest at a lower level or not at all" to be an "inhibitor or activator of a protein," and an inhibitor or activator of a POI may alter the biological activity of the POI through a direct POI-binding mechanism or an

indirect pathway-binding mechanism. The word "bind" or "binding" appears nowhere in the '281 patent in conjunction with an "inhibitor or activator of a protein."

At oral argument (and thus on the late side of things), Housey produced definitions of "inhibitor" and "activator" from technical dictionaries to argue for the first time on appeal that the plain meaning of an "inhibitor or activator of a protein" is limited to a substance that binds to the protein. With respect to an inhibitor or activator of an *enzyme,* these definitions do include a direct-binding limitation. *See Chambers Dictionary of Science and Technology* 13 (1999) (defining "activator" as "[o]f an enzyme, a small molecule which binds to it and increases its activity"); *Henderson's Dictionary of Biological Terms* 284 (11th ed.1995) (defining "inhibitor" as "a substance which . . . prevents the normal action of an enzyme . . . by binding to the active site . . . [or] by binding to other parts of the enzyme"). However, the claim language is an "inhibitor or activator of a protein," not of an enzyme,[3] and the dictionaries also include a more appropriate general definition of both "activator" and "inhibitor" that requires only an effect on the biological activity of the protein, regardless of the mechanism used to achieve that effect. *See Chambers Dictionary of Science and Technology* 13 (defining "activator" as "[a]ny agent . . . whose presence stimulates biochemical or physiological changes"); *Henderson's Dictionary of Biological Terms* 284 (defining "inhibitor" as "any agent which checks or prevents an action or process"). Thus, according to the evidence submitted by Housey, the plain meaning of "inhibittor or activator of a protein" does not support the inclusion of the direct-binding concept as a limitation on the claimed method.

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[3] Enzymes are only one of many types of proteins. *See Henderson's Dictionary of Biological Terms* 474 (noting that proteins are "[e]ssential in living organisms as enzymes, structural constituents of cells and tissues and in control of gene expression etc.").

The intrinsic evidence of the '281 patent does not clearly disavow this broad plain meaning. In fact, even if the plain meaning were considered to be ambiguous, supporting both a narrower definition limited to inhibitors and activators that bind to the POI and a broader definition of inhibitors and activators that need only affect the biological activity of the POI, the district court was correct because the specification and prosecution history affirmatively demonstrate that Housey intended the broader meaning that is not limited to direct binding.

The specification foresaw the possibility of a substance affecting the "responsive change in a phenotypic characteristic" in the cell line with the greater amount of POI without the substance binding to the POI. *See* '281 patent, col. 6, ll. 29-33 ("[C]ell lines will be sensitive in their growth properties [i.e. in the their relevant phenotypic characteristic] to chemical agents which are capable of binding to, *or modifying the biological effects of,* the POI." (emphasis added)).[4] The specification also expressly defines the terms "inhibitors" and "activators" in terms of the biological activity of the POI without any reference to binding. *See id.* at ll. 40-42 ("The term 'inhibitors' includes both substance[s] which reduce the activity of the POI and th[o]se which nullify it altogether."); *id.* at ll. 37-40 ("The term 'activators,' as used herein, includes both substances necessary for the POI to become active in the first place, and substances which merely accentuate its activity.").

Housey's statements in the prosecution history of the '281 patent also support this conclusion. In distinguishing prior art

[4] Housey's argument that the "or" in this passage from the specification is explanatory, not disjunctive, is strained. "Binding to" is unquestionably narrower than "modifying the biological effects of." Rarely does one use "or" in the explanatory sense to define a word as simple as "bind," and even less frequently does one use a broad, general term to explain the meaning of a narrow, precise term.

during prosecution, Housey repeatedly characterized his invention as one that could determine whether a substance interacted with the biological pathway in which a particular protein functioned: The prior art did "not provide the *target protein/biochemical pathway specificity* of the present invention." Because biological pathways usually involve more than one protein, a substance can clearly interact with the POI's biological pathway without binding with the POI itself, and Housey stated as much in the process of distinguishing another prior art reference:

> Substances . . . identified or characterized using the teachings of the Housey patents will be found to interact directly with the target protein itself and/or with other proteins in which the target protein also interacts in the form of dimeric or multimeric complexes. In this fashion, the approach disclosed in the Housey patents provides a *specificity* between a target protein and its attendant biochemical pathways within the cell that is impossible to achieve with other assay systems.

Housey argues that an inhibitor or activator is limited to substances that bind to the POI because the claim language specifies an inhibitor or activator "of a protein." The fact that the biological activity "of a protein" is affected by a screened substance, however, lends no insight into whether the effect must be attributed to binding to the protein or some other type of influence on the biological pathways through which the protein is created and in which the protein functions.

Similarly, Housey argues that the recurring presence of the terms "specific" and "specifically" in the specification and the prosecution history conclusively demonstrates that the inhibitor or activator operates by binding with the POI. *See, e.g.*, '281 patent, col. 1, ll. 10-12 ("In particular, [the invention] is concerned with a method of screening for substances which *specifically* inhibit or activate a particular protein." (emphasis added)); *id.* at col. 2, ll. 27-28 (describing

the invention as having a "specificity for detecting an active agent exceeding that of" the prior art assays); *id.* at ll. 28-32 ("[T]he method which we describe herein involves the generation of a cell line purposefully engineered to detect both stimulatory and inhibitory agents which are absolutely *specific* for any given protein which affects the cultural of morphological characteristics of a cell." (emphasis added)); *id.* at col. 9, ll. 30-31 (stating that the method was screening for "substances which may contain biologically active agents *specific* to the POI" (emphasis added)). Leaving aside the absence of the word "specific" in the claim language (and our repeated warnings not to import limitations from the specification that are not present in the claims, *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1325 (Fed. Cir.2003) ("The danger of improperly importing a limitation is even greater when the purported limitation is based upon a term not appearing in the claim.")), this language from the specification does not lead to a strong inference of direct binding to the POI. As the above-quoted sections of the prosecution history demonstrate, the use of "specific" suggests equally as strongly that the biological activity of the POI is affected, through a direct or indirect mechanism, when the biological activity of other proteins in other biochemical pathways is not. Furthermore, the specification, too, equates specificity with the biological effect of the inhibitor or activator, not with any particular mechanism of action. *See* '281 patent, col. 3, ll. 5-10 ("Substances which *specifically* inhibit or inactivate the POI may be distinguished from substances which affect cell morphology or growth by other mechanisms in that they will have a greater effect on the test lines than on the control line." (emphasis added)).[5]

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[5] Housey's reference to the definition of the term "specific binding" is not relevant to the use of "specific" in the patent, as "specific binding" presupposes the presence of binding, the very limitation which is in question here.

Finally, Housey points to language at the end of one of the specific embodiments in the specification and argues that it demonstrates that the patented assay must be able to detect substances that bind to the POI: "[T]his work establishes, for the first time, the fact that stable overproduction of a protein in mammalian cells can result in a novel cellular phenotype(s) . . . which can be directly modulated by chemical agents *which interact with the protein*." *Id.* at col. 18, ll. 30-36 (emphasis added). First, this passage does not indicate that the interaction between the agent being screened and the POI must be in the form of direct binding; another protein or cellular component may provide the mechanism through which the agent interacts with the POI. Second, not only does this passage describe only a single embodiment (and limitations on specific embodiments are not to be imported into the claims, *see Electro Med. Sys., S.A. v. Cooper Life Scis., Inc.*, 34 F.3d 1048, 1054 (Fed. Cir.1994)), but it describes an embodiment in which there is "a direct relationship between the molar amount of inhibitor [or activator] required to prevent [or stimulate] [the phenotypic response] and the molar amount of [the POI] present in each cell line." '281 patent, col. 18, ll. 22-24, 28-30. This additional fact notes a direct relationship between the amount of POI overexpressed in the test cell and the amount of inhibitor or activator required to eliminate the "responsive change in a phenotypic characteristic." If true, this fact may or may not permit one of skill in the art to use the claimed method to divine that the inhibitor or activator binds directly to the POI, but it unquestionably is not a claimed limitation in the "method of determining whether a substance is an inhibitor or activator of a protein" of claim 1 of the '281 patent.

C

Housey invokes two canons of claim construction to support limiting an "inhibitor or activator of a protein" to a substance that binds to that protein, but neither is persuasive.

First, Housey cites *Athletic Alternatives, Inc. v. Prince Manfacturing, Inc.*, 73 F.3d 1573, 1581 (Fed. Cir.1996), for the proposition that in the event of a tie between a broader and narrower meaning, the notice function of patent law requires that the narrower meaning prevails. Housey misreads *Athletic Alternatives*. In that unusual case, one patent applicant made two *contradictory* and *irreconcilable* affirmative representations of the contested limitation. In those circumstances, we held that the narrower interpretation trumps the broader interpretation. In this case, there are no contradictory and irreconcilable choices for the meaning of "inhibitor or activator of a protein." Second, Housey relies on the axiom that "[c]laims should be so construed, if possible, as to sustain their validity." *Rhine v. Casio, Inc.*, 183 F.3d 1342, 1345 (Fed. Cir.1999) (quoting *Carman Indus., Inc. v. Wahl*, 724 F.2d 932, 937 n. 5 (Fed. Cir.1983)). Here, we have not been asked to review validity, and the district court did not pass on validity. Housey's stipulation of invalidity alone is insufficient to invoke this canon. In any event, the canon lacks dispositive effect in this case. *See Liebel-Flarsheim Co.*, 358 F.3d at 911 ("[U]nless the court concludes, after applying all the available tools of claim construction, that the claim is still ambiguous, the axiom regarding the construction to preserve the validity of the claim does not apply.").

IV

We agree with the district court's construction of the "activator or inhibitor of a protein" limitation, and we therefore affirm the judgment of the district court.

COSTS

No costs.

AFFIRMED.

PAULINE NEWMAN, *Circuit Judge*, dissenting.

It is time to restore the law of claim construction to a more apt wisdom and more usable simplicity. The only issue in this case is the construction of the phrase "inhibitor or activator of a protein." My colleagues' approach to construction is based on confusing recent pronouncements of panels of this court, contravening earlier statements of precedent, thus adding to the confusion.

I

The panel majority propounds the rule that the "plain and ordinary meaning of the claim language" should be used to define the scope of the claims unless the inventor "has explicitly disclaimed or clearly disavowed this meaning." Maj. op. at 1351-1352. The panel majority states that absent such disclaimer, claims are "inimical to any narrower construction." Maj. op. at 1352. Precedent is exactly contrary: a claim is "inimical" to any broader construction than the invention set forth in the specification, and reliance on dictionaries, even technical dictionaries, without due consideration of the context of the invention may lead to "absurd results":

> Indiscriminate reliance on definitions found in dictionaries can often produce absurd results. Words are used in many senses and often have diametrically opposed meanings, depending upon the sense in which they are used. One searching for the dictionary definitions of 'effectively' or 'effect' will find among the numerous definitions listed many which are indisputably inapplicable to the instant use of the word 'effectively.' But the words in which a claim is couched may not be read in a vacuum. One need not arbitrarily pick and choose from the various accepted definitions of a word to decide which meaning was intended as the word is used in a

> given claim. The subject matter, the context, etc., will more often than not lead to the correct conclusion.

Liebscher v. Boothroyd, 46 C.C.P.A. 701, 258 F.2d 948, 951 (1958). *See also e.g., Netword, LLC v. Centraal Corp.*, 242 F.3d 1347, 1352 (Fed. Cir.2001) ("The claims are directed to the invention that is described in the specification; they do not have meaning removed from the context from which they arose."); *Toro Co. v. White Consol. Indus., Inc.*, 199 F.3d 1295, 1299 (Fed. Cir.1999) ("[W]ords of ordinary usage must nonetheless be construed in the context of the patent documents. Thus the court must determine how a person of experience in the field of this invention would, upon reading the patent documents, understand the words used to define the invention."); *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir.1998) ("[A] common meaning, such as one expressed in a relevant dictionary, that flies in the face of the patent disclosure is undeserving of fealty. . . . [T]he interpretation to be given a term can only be determined and confirmed with a full understanding of what the inventors actually invented and intended to envelop with the claim."). Claims to an invention that is not described in the specification are an anachronism. Many inventions concern complex and detailed technology, and the terse style of the patent claim is not a replacement for the elaboration in the written description. The claims are the concluding portion of the specification, and their statutory function is "particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." 35 U.S.C. § 112. A claim has no meaning out of the context of the invention that is described, enabled, and prosecuted.

This case again illustrates the conflict generated in the court's recent jurisprudence of claim construction. The panel majority reinforces the recently created dominance of general definitions, wherein the court created a "heavy presumption" in contravention of precedent. It is an established rule of the

construction of legal documents that technical terms are presumed to have the meaning of the technical field of the document, not a "general meaning." Technical terms take their meaning from the technology and context in which they are used, not from general usages of the same word. Thus terms in patent claims are understood in the technical/scientific context of the specification; the presumption is that they have their technical meaning, not a general meaning.

This same interpretive rule applies to statutes, contracts, deeds, patents, and other legal documents. *See, e.g.*, 2A Norman Singer, *Sutherland Statutory Construction* § 47:29 (6th ed. 2000) ("In the absence of legislative intent to the contrary, or other overriding evidence of a different meaning, technical terms or terms of art used in a statute are presumed to have their technical meaning. If a term is connected with and used with reference to a particular trade, the term will have the meaning given [by] experts in the particular trade.") (footnotes omitted).

It is curious indeed to announce a "heavy presumption" that the meaning of a term in a patent claim is unencumbered by the specification, and to place a "heavy burden" on overcoming that presumption. Such a presumption dissociates the term from the invention described, enabled, and prosecuted by the inventor, and places an unnecessary burden on the inventor who wants simply to restore the meaning that the inventor and the examiner, and others in the field of the invention, clearly understand. I thus state my respectful disagreement with the panel's reinforcement of the distortions that have entered this court's jurisprudence. The written description is not an also-ran in claim construction, as the panel states; it is the primary resource in understanding the claims.

Patent claims are stated in words, and words can have a non-technical as well as a technical meaning. The words "inhibit" and "activate" are good examples of such words,

invoking the rule that their specific meaning is derived from the field of their usage, upon inspection of the patent specification and the prosecution history. *See, e.g., Toro*, 199 F.3d at 1299-1300 ("In judicial 'claim construction' the court must achieve the same understanding of the patent, as a document whose meaning and scope have legal consequences, as would a person experienced in the technology of the invention.'"), *further appeal*, 266 F.3d 1367 (Fed. Cir. 2001). The *Toro* court recognized that "dictionary definitions of common words are often less useful than the patent documents themselves in establishing the usage of ordinary words in connection with the claimed subject matter." *Id.* at 1300 (each party relying on a different dictionary definition that favored its position).

The rule is that claims are viewed and understood in light of the specification, of which they are a part. *See, e.g., Multiform Desiccants, Inc. v. Medzam, Ltd.*, 133 F.3d 1473, 1478 (Fed. Cir.1998) ("The best source for understanding a technical term is the specification from which it arose, informed, as needed, by the prosecution history."). If there is a "presumption" in claim construction, it is that a claim term has the meaning ascribed by the patent documents. It is incorrect to impose the obverse "heavy presumption" that the dictionary definition dominates and all inapplicable variants must be expressly disclaimed. The role of dictionaries and treatises is to educate the non-technical judge in understanding what the inventor and the examiner understood, not to impose a new evidentiary presumption and not to enlarge the patented invention beyond that set forth by the inventor. The words of patent claims have the meaning and scope with which they are used in the specification and the prosecution history.

It is also incorrect to hold that words in claims are broader in meaning than their usage in the specification, simply because a dictionary definition may not contain the limi-

tations of the specification. It is imprecise to state that claims are not limited by "a narrow specification" unless the inventor expressly so limits them, maj. op. at 1352, for the specification always limits the claims. The claims are part of the specification; their role is to point out what is covered by the patent, not to broaden the text. *See, e.g., Dow Chemical Co. v. Sumitomo Chemical Co.*, 257 F.3d 1364, 1378 (Fed. Cir.2001) (claim scope is limited to the meaning set forth in the patent documents).

The panel thus perpetuates a distortion of the construction of patent documents, contrary to precedent and defeasible of the critical need for stability and predictability in the system of patents.

II

This case turns on whether the claim clause "inhibitor or activator of a protein" requires direct interaction with the protein. My colleagues on this panel rely on a general understanding of the word "specificity" to decide that the claims cover all forms of indirect interactions and are therefore invalid. The specification, on its face, can support either theory, but does not support the majority's ruling that Housey's proposed limitation of the term "inhibitor or activator" is "inimical" to the majority's proposed "plain meaning" taken from general dictionaries. It is noteworthy that the majority's proposed "plain meaning" differs from the specification's statement of the invention.

The patent documents state that the invention concerns "direct modulation," and that the prior art shows primarily "indirect modulation" of intermediate agents. The defendants dispute this statement. The patentee buttresses its position with selections from the specification, for example:

> Thus, this work establishes, for the first time, the fact that stable overproduction of a protein in mammalian cells can result in a novel cellular phenotype(s) . . .

> which can be directly modulated by chemical agents which interact with the protein.

'281 patent, col. 18, lines 30-36:

> In particular, it is concerned with a method of screening for substances which specifically inhibit or activate a particular protein, especially in a manner apparent to the naked eye.

'281 patent, col. 1, lines 10-12. The defendants cite other, broader statements.

Both sides cite dictionaries and technical treatises that support their respective positions, Housey citing the *Textbook of Receptor Pharmacology* 123 (John C. Foreman & Torben Johansen eds., 1996) for its statement that:

> An all-important consideration in binding studies is the extent to which the measured binding of a radioligand represents association with the receptor or other site of interest. In functional studies there is no difficulty, the response can only be elicited by the binding of an agonist [activator] to the receptor and for an antagonist [inhibitor] to inhibit the response to an agonist it must also bind to the receptor (or a site coupled to it). Invariably, in binding studies there is uptake of the radioligand by other tissue components (unless, of course, binding to a purified, soluble protein is under investigation). The binding to the receptor is normally termed specific binding, whereas the binding to non-receptor tissue components is referred to as nonspecific binding.

The prosecution of the '007 patent referred to the specificity of direct binding; for example, Dr. Housey told the examiner:

> Substances so identified or characterized using the teachings of the Housey patents will be found to interact

> directly with the target protein itself and/or with other proteins which the target protein also interacts in the form of dimeric or multimeric complexes. In this fashion, the approach disclosed in the Housey patents provides a specificity between a target protein and its attendant biochemical pathways within the cell that is impossible to achieve with other assay systems.

Declaration of Gerard M. Housey under 37 C.F.R. § 1.132 at ¶ 14, October 22, 1996.

In a related proceeding involving these patents, [Housey's] expert Dr. Griffin submitted a declaration to the court stating that the terms "specific" and "specifically" are used to characterize a substance that binds to a target protein. Declaration of Dr. James Griffin at 1, June 7, 2002, *Bayer AG v. Housey Pharms., Inc.*, No. 01-148 (D. Del. filed March 6, 2001). On the other hand, Bayer's expert Dr. Roninson provided evidence during a deposition as follows:

> Q. As a scientist, when you see the term "specific inhibitor," do you not understand that to mean substance is binding to the protein?
> A. No, I don't.

Deposition of Igor B. Roninson at 42, June 19, 2002, *Bayer AG v. Housey Pharms., Inc.*, No. 01-148 (D. Del. filed March 6, 2001). But Bayer's expert Dr. Fields stated that "one aspect of being a specific activator or inhibitor is that it binds directly to that protein of interest. . . ." Deposition of Alan P. Fields at 91, July 2, 2002, *Bayer AG v. Housey Pharms., Inc.*, No. 01-148 (D. Del. filed March 6, 2001). And defendants' expert Dr. Silverstein stated before the district court in this litigation that "[a]lthough . . . [drug discovery] programs may include cell-based assays, for the reasons stated above, they must include cell-free assays in order to determine whether or not there is a direct interaction between the test substance and the protein of interest."

Declaration of Professor Saul J. Silverstein at ¶ 22, August 28, 2002, *Housey Pharms., Inc. v. Astrazeneca UK Ltd.*, No. 01-CV-401 (D.Del. November 27, 2002).

This conflicting expert testimony requires resolution by the court, but such resolution must be consistent with the subject matter that was invented, described and enabled. Reliance on dictionaries does not achieve this purpose. In addition, when it is reasonable to do so, claims should be construed so as to preserve their validity. *See Wang Labs. Inc. v. America Online Inc.*, 197 F.3d 1377, 1382 (Fed. Cir.1999) (claims should be construed, when reasonably possible, to sustain their validity).

On correct guidance of the principles of claim construction, I would remand for resolution of conflicting scientific evidence, and re-determination of the meaning and scope of the correctly construed claim.

APPENDIX B

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

C.A. No. 01-401-SLR

HOUSEY PHARMACEUTICALS, INC.,
Plaintiff,

v.

ABBOTT PHARMACEUTICALS, INC., *et al.*,
Defendants.

FINAL JUDGMENT ORDER

WHEREAS the parties have entered into a Stipulation and Order of Invalidity and Non-Infringement; and

WHEREAS the Court has entered a claim construction order in *Bayer v. Housey Pharmaceuticals,* 01-148 (SLR) dated November 12, 2002 which also applies in this action.

IT IS HEREBY ORDERED this 27th day of November, 2002 that final judgment of invalidity and noninfringement of United States Patent Nos. 4,980,281, 5,266,464, 5,688,655 and 5,877,007 ("the patents in suit") is hereby entered in favor of the stipulating defendants[6] in accordance with the terms of the Stipulation and Order of Invalidity and Non-Infringement.

/s/ Sue L. Robinson
United States District Judge

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[6] AstraZeneca UK Ltd., AstraZeneca LP, AstraZeneca Pharmaceuticals LP, Aventis Pharmaceuticals, Inc., Bristol-Myers Squibb Company, Merck & Co., Inc., Roche Holdings, Inc., Hoffmann-La Roche Inc., Roche Laboratories, Inc., Syntex (U.S.A.) Inc., Wyeth and Wyeth Pharmaceuticals, Inc.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

C.A. No. 01-401-SLR

HOUSEY PHARMACEUTICALS, INC.,
Plaintiff,

v.

ABBOTT PHARMACEUTICALS, INC., *et al.*,
Defendants.

STIPULATION AND ORDER OF INVALIDITY AND NON-INFRINGEMENT

Plaintiff, Housey Pharmaceuticals, Inc. ("Housey"), and AstraZeneca UK Ltd., AstraZeneca LP, AstraZeneca Pharmaceuticals LP, Aventis Pharmaceuticals, Inc., Bristol-Myers Squibb Company, Merck & Co., Inc., Roche Holdings, Inc., Hoffmann-La Roche Inc., Roche Laboratories, Inc., Syntex (U.S.A.) Inc., Wyeth and Wyeth Pharmaceuticals, Inc., (collectively, the "Defendants") by their undersigned counsel, hereby stipulate and agree, subject to the approval of the Court as follows:

1. This is a patent infringement suit brought by Housey in which Housey claims that Defendants have infringed the claims of U.S. Patent Nos. 4,980,281, 5,266,464, 5,688,655 and 5,877,007 ("the patents in suit").

2. Defendants have counterclaimed that, *inter alia*, the patents in suit are invalid, unenforceable, and not infringed.

3. On November 12, 2002, the Court entered a Memorandum Order regarding claim construction in the co-pending matter styled *Bayer AG v. Housey Pharmaceuticals, Inc.*, C.A. No. 01-148 SLR, attached hereto as Exhibit A.

4. For purposes of judicial economy and based upon the Court's construction of the claim limitation "inhibitor or activator of a protein," Housey hereby stipulates, subject to its right to appeal the Court's claim construction and any final judgment based thereon, that the Court may enter an order stating that the patents in suit are invalid and not infringed.

5. For purposes of judicial economy and based upon the Court's construction of the claim limitation "phenotypic characteristic," Housey hereby stipulates, subject to its right to appeal the Court's claim construction and any final judgment based thereon, that the Court may enter an order stating that the claims of the patents in suit are not infringed by five sets of the defendants (AstraZeneca UK Ltd., AstraZeneca LP, AstraZeneca Pharmaceuticals LP, Aventis Pharmaceuticals, Inc., Bristol-Myers Squibb Company, Merck & Co., Inc., Roche Holdings, Inc., Hoffmann-La Roche Inc., Roche Laboratories, Inc., Syntex (U.S.A.) Inc.).

6. The parties reserve all their rights to argue on appeal that the Court's construction of the other claim limitations should be affirmed, reversed or modified.

7. For purposes of judicial economy, assuming that the Court's Final Judgment Order in this action is affirmed on appeal and the action is not remanded, Defendants will not assert in this action their remaining counterclaims against Housey, specifically, their counterclaims for unenforceability and their counterclaims for attorneys fees.

8. The parties therefore agree to the entry of the attached Final Judgment Order as to both Housey's claim for infringement and Defendants' counterclaims for invalidity and non-infringement. It is provided, however, as to the five sets of defendants identified in

paragraph 5, that: (a) in the event that the Court's determinations on both issues of claim construction set forth in paragraphs 4 and 5 above are reversed or modified on appeal such that the matter is remanded for further consideration, Housey and the five sets of defendants reserve all of their claims, counterclaims, arguments and defenses; and (b) if either of the claim construction issues set forth in paragraphs 4 and 5 above is affirmed on appeal, Housey and the five sets of defendants agree that there is no issue of infringement, validity, or enforceability remaining to be tried. It is further provided, as to defendants Wyeth and Wyeth Pharmaceuticals, Inc., (collectively, "Wyeth"), that: (a) in the event that the Court's determination on the issue of claim construction set forth in paragraph 4 above is reversed or modified on appeal such that the matter is remanded for further consideration, Housey and Wyeth reserve all of their claims, counterclaims, arguments and defenses; and (b) if the claim construction issue set forth in paragraph 4 is affirmed on appeal, Housey and Wyeth agree that there is no issue of infringement, validity, or enforceability remaining to be tried.

9. All declaratory judgment counterclaims are dismissed without prejudice as moot.

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SO ORDERED this ____ day of November, 2002

_____
United States District Judge

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

Civil Action No. 01-148-SLR

BAYER AG and BAYER CORPORATION,
Plaintiffs,

v.

HOUSEY PHARMACEUTICALS, INC.,
Defendant.

MEMORANDUM ORDER

At Wilmington this 12th day of November, 2002, having heard oral argument and having reviewed papers submitted in connection therewith;

IT IS ORDERED that the disputed claim language in United States Patent Nos. 4,980,281; 5,266,464; 5,688,655 and 5,877,077, as identified by the above referenced parties, shall be construed as follows, consistent with the tenets of claim construction set forth by the United States Court of Appeals for the Federal Circuit:

A. "A Method of Determining"

The parties agree that, in science, rarely is anything 100% certain. Consistent with this understanding, the patent specification, and the prosecution history,[7] "determining" shall be construed to mean "ascertaining with a high degree of probability that an unknown or suspected substance is an activator or inhibitor of a target protein."

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[7] The patentee's 37 C.F.R. § 1.132 declaration states that "the predictive ability of the claimed cell-based system is far higher than that for more traditional cell-free systems." (D.I. 276, Ex. B)

B. "Inhibitor or Activator of a Protein"

The claim language, the specification, and the prosecution history contain no language limiting an activator or inhibitor to substances that directly bind to the target protein. As such, the court rejects the patentee's attempt to read such a limitation into the claims.[8] Thus, the term "inhibitor or activator" shall be construed to mean "a substance that has a greater effect on the phenotype of cells that express the protein of interest at a higher level than on the phenotype of cells that express the protein of interest at a lower level or not at all." ('281 patent, col. 3, 11. 5-10; col. 4, 11. 48-50)

C. "Phenotypic Characteristic"

The term "phenotypic characteristic" shall be construed to mean "an observable trait of a cell and does not include characteristics of a temporary or transient nature, such as, for example, the levels or concentrations of ions or other chemical substances." The patent specification states "[t]he phenotypic characteristic is preferably a 'cultural' or 'morphological' characteristic of the cell." ('281 patent, col. 4, 11. 54-55) Cultural or morphological changes are stable, non-transient traits.

D. "Phenotypic Response" or "Responsive Change in a Phenotypic Characteristic"

The term "phenotypic response" or "responsive change in a phenotypic characteristic" shall be construed to mean "the characteristic which is changing and which the person

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[8] The patentee has argued that the term should be construed to mean "substances the directly interact, i.e., bind to, the target protein." The court, however, finds no intrinsic evidence to support the direct interaction (binding) limitation. The extrinsic evidence (expert reports) submitted by the patentee are merely conclusory.

skilled in the art is measuring, which is reflective of the activation or inhibition of the protein of interest."[9]

E. "Evokes," "Exhibits," and "Induces"

The term "evokes," "exhibits," and "induces" shall be construed to mean "the phenotypic change in the cell that overproduces the protein of interest is observable prior to the addition of the test substance to that cell." ('464 patent, col 7, 11, 7-15)

/s/ Sue L. Robinson
United States District Judge

[9] The court rejects plaintiffs' attempt to add language regarding reporter genes to the claim construction. Although the "responsive change" must be reflective of the activation or inhibition of the protein of interest, there is no limitation as to how the "responsive change' may be measured. ('655 patent, claim 1)

APPENDIX C

UNITED STATES COURT OF APPEALS
FEDERAL CIRCUIT

Nos. 03-1193, -1210

HOUSEY PHARMACEUTICALS, INC.,
Plaintiff-Appellant,

v.

ASTRAZENECA UK LTD., ASTRAZENECA LP, ASTRAZENECA PHARMACEUTICALS LP, and AVENTIS PHARMACEUTICALS, INC.,
Defendants-Cross Appellants,

and

BRISTOL-MYERS SQUIBB COMPANY,
Defendant-Cross Appellant,

and

MERCK & CO., INC.,
Defendant-Cross Appellant,

and

ROCHE HOLDINGS, INC., HOFFMANN-LA ROCHE INC., ROCHE LABORATORIES, INC., and SYNTEX (U.S.A.) INC.,
Defendants,

and WYETH AND WYETH PHARMACEUTICALS, INC.,
Defendants-Cross Appellants.

ORDER

A combined petition for panel rehearing and for rehearing en banc having been filed by the APPELLANT, and the petition for rehearing having been referred to the panel that

heard the appeal, and thereafter the petition for rehearing en banc having been referred to the circuit judges who are in regular active service,

UPON CONSIDERATION THEREOF, it is

ORDERED that the petition for panel rehearing be, and the same hereby is, DENIED and it is further

ORDERED that the petition for rehearing en banc be, and the same hereby is, DENIED.

The mandate of the court will issue on September 1, 2004.

FOR THE COURT,
Jan Horbaly
Clerk

Dated: August 25, 2004

cc: R. Terrance Rader
W. Lee, J. Lynch, H. Schwartz, R. Baechtold

HOUSEY PHARMACEUTICAL V ASTRAZENECA, 03-1193, -1210 (DCT – 01-CV-401)